

The Impact of Competitive Processes on Controlled Radical Polymerization

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Abstract

The kinetics of radical polymerization have been systematically studied for nearly a century and in general are well understood. However, in the light of recent developments in controlled radical polymerization many kinetic anomalies have arisen. These unexpected results have been largely considered separate and various, as yet inconclusive, debates as to the cause of these anomalies

are ongoing. Herein we present a new theory on the cause of changes in kinetics under controlled radical polymerization conditions. We show that where the fast, intermittent deactivation of radical species takes place, changes in the relative rates of the competitive reactions that exist in radical polymerization can occur. To highlight the applicability of the model we demonstrate that the model explains well the reduction in branching in acrylic polymers in RAFT polymerization. We further show that such a theory may explain various phenomena in controlled radical polymerization and may be exploited to design precise macromolecular architectures.

Introduction

The fundamental basis of the mathematical description of most chemical reaction kinetics is that the rate of any given reaction can be described as a function of a rate coefficient, or series of rate coefficients, and the concentration of the species involved in the reaction such that, for example, $A+B \rightarrow C$ can be described by $\frac{d[C]}{dt}=k[A][B]$. The use of this simple yet essential concept is so widespread that it is taught across the educational spectrum and has been applied to every scientific discipline. However, it is key to point out that this method is based on an intrinsic assumption that the process is memoryless and hence the probability density function, that is the distribution of possible reaction times, follows an exponential decay. This assumption is generally valid but it is questionable under certain circumstances that will be detailed herein. In this article, we aim to show that in radical polymerizations, particularly in controlled radical polymerization where the radical intermediate is intermittently deactivated, substantially different kinetic features that cannot be explained using an exponentially decaying

probability distribution are in effect. In order to illustrate the point, radical polymerization of acrylic monomers is considered.

In polymerization of acrylic monomers, transfer to polymer is a particularly important kinetic event that impacts heavily on both the rate of polymerization and on the microstructure of the polymer.¹⁻¹² Transfer to polymer in acrylic monomers has been shown to be mainly due to intramolecular transfer via a six membered ring transition state, resulting in a mid chain radical.¹³⁻¹⁷ In general, for most polymerizations which are conducted at a temperature of <100 °C, the most likely fate of the midchain radical is propagation, leading to the formation of quaternary carbons that are a fingerprint of this process and can be detected by ¹³C NMR.^{13,18} The considerably lower reactivity of the formed tertiary radicals in comparison to secondary radicals results in a decrease of the effective propagation rate constant.^{1,2,6,19} This has been cited as the cause for the inability to accurately measure the propagation rate coefficient, k_p of acrylic monomers by pulsed laser polymerization except for at low temperatures, where backbiting is significantly reduced,^{4,20-22} and, additionally, the reason why the measurement of k_p in the absence of backbiting results in a value that is unable to describe polymerization kinetics in conditions where backbiting is significant.² Because most of the branches are formed by backbiting, in the homopolymerization of acrylate monomers the formation of branches can be described by Scheme 1. The propagating secondary radical, R_2^* , undergoes intramolecular chain transfer to polymer via a six membered ring transition state and subsequent propagation from the formed tertiary radical, R_3^* , with rate constant k_{p3} ($k_{p3} \ll k_p$) to form a branch point. According to this scheme, the branching fraction, defined as the fraction of acrylate units that have a quaternary carbon, calculated using classical kinetics is:

$$\text{Branching fraction} = \frac{k_{p3} [R_3^\bullet] [M]}{k_p [R_2^\bullet] [M] + k_{p3} [R_3^\bullet] [M]} \quad (1)$$

where $[R_2^\bullet]$ and $[R_3^\bullet]$ are the concentrations of the secondary and tertiary radicals, respectively. Under quasi steady state conditions

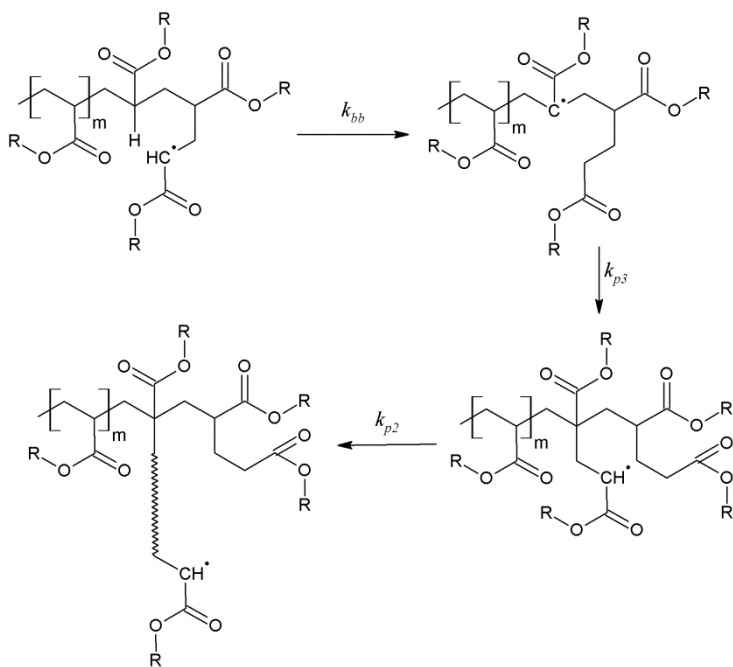
$$k_{p3} [R_3^\bullet] [M] = k_{bb} [R_2^\bullet] \quad (2)$$

and combination of Equations 1 and 2 yields

$$\text{Branching fraction} = \frac{k_{bb}}{k_p [M] + k_{bb}} \quad (3)$$

which predicts an instantaneous branching fraction independent of any additional factors.

Scheme 1 Branch formation by intramolecular chain transfer to polymer in radical polymerization of acrylates.



The variation in monomer content throughout the polymerization process results in a change to the instantaneous branching fraction. ^{13}C NMR experiments yield the cumulative value of this variable. The branching fraction, as defined by Equation 3, can also be regarded as the measurable probability of backbiting occurring over propagation. It is important to distinguish between this probability and the probability density function which describes the instantaneous distribution of potential times a given reaction will take to occur. This distribution serves to reflect the fact that while reactions occur with an average frequency (for backbiting the average time to reaction is $1/k_{bb} \approx 1000 \mu\text{s}$) there is a probability that the reaction can occur at longer or shorter time. The measurable probability of backbiting results from the interplay between the probability density functions of propagation and backbiting. An example in the evolution of measurable probability of backbiting over the course of the reaction time and the probability density distributions are shown in Figure 1 for a batch process. Figure 1 shows that in a batch process, the measurable backbiting increases during the whole process (as $[\text{M}]$ decreases) and most of the backbiting occurs at high monomer conversions. Figure 1 also presents the normalized probability density functions applied in classical kinetics for propagation (squares, $p_p(t) = k_p[\text{M}] \exp(-k_p[\text{M}]t)$) and backbiting (circles, $p_{bb}(t) = k_{bb} \exp(-k_{bb}t)$) at high and low conversions. It can be seen that the probability density functions vary along the process.

It is important to note that the probability density distribution, being a fundamental characteristic of a given reaction process, is independent of any competitive reactions and in the view of classical kinetics is given by an exponentially decaying function defined only by the rate constant and concentrations of species involved. The use of this exponentially decaying function is implicit every time one uses a rate constant and whether or not this function accurately

describes the true situation in radical reactions is the critical point in this article. On the other hand, the measurable probability, which in this case is the instantaneous branching fraction, is affected by competitive reactions and can take a variety of forms that vary with the total reaction time. Note that changes in the measurable probability are on the order of minutes or hours in contrast to the probability density distributions which for radical reactions are typically up to 10 ms.

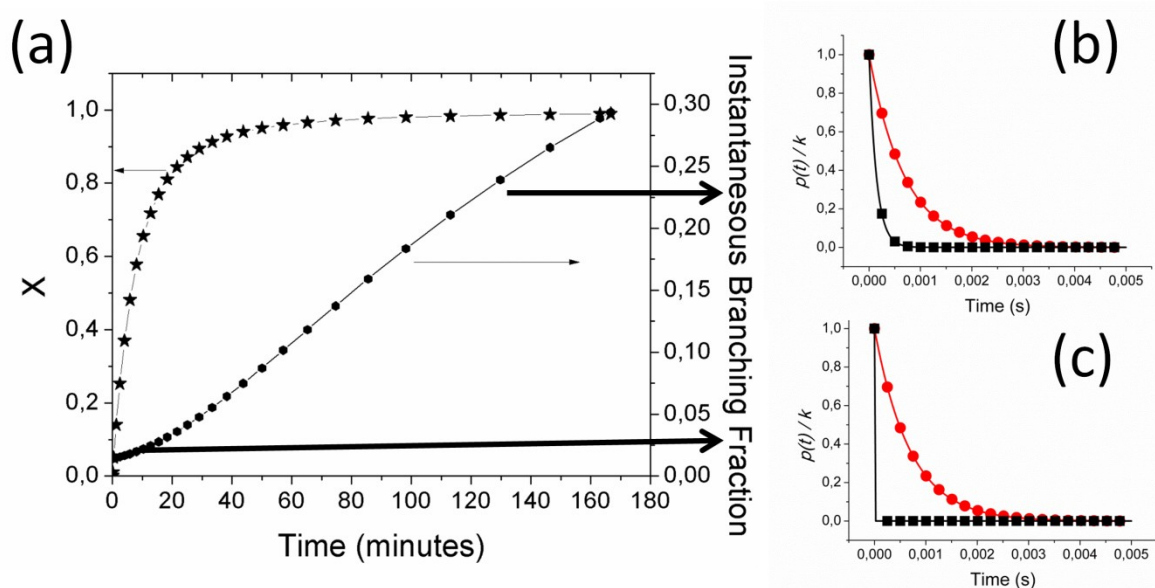


Figure 1 (a) Change in instantaneous branching fraction calculated from Equation 3 and conversion with process time for a typical bulk radical polymerization of n-butyl acrylate (for detailed kinetic model see ref ²³). Figures on the right show for low conversion (c) and high conversion (b), the probability density distributions for propagation (squares, $p_p(t) = k_p[M] \exp(-k_p[M]t)$) and backbiting (circles $p_{bb}(t) = k_{bb} \exp(-k_{bb}t)$). In order to fit both functions in the same plot, $p(t)/k$ is presented, where $k = k_p[M]$ for propagation and $k = k_{bb}$ for backbiting.

While this currently accepted description of backbiting and branch formation, described above, is useful for interpreting results from polymerization of acrylic monomers both in bulk and

solution, and in fact a value for the rate constant of backbiting, k_{bb} , has previously been estimated,^{8,10,24–27} some curious anomalous observations are seemingly impossible to align with such a description. For example, in controlled radical polymerization and in the presence of high concentrations of chain transfer agent, branching fraction has been shown to be significantly reduced.^{28–33} In addition, it has been shown experimentally that it is possible to obtain accurate k_p values from pulsed laser polymerization (PLP) experiments at moderate temperatures when a high frequency pulse is used, thus suggesting branching can be limited at high frequency pulses.³⁴ It should be noted that all of the above processes introduce a competition between kinetic events, either from the reversible deactivation of active chains, from chain transfer to CTA, or from termination induced by laser pulsing, that is not present in a conventional radical polymerization reaction.

For controlled radical polymerization it was initially postulated that the differences in the concentrations of highly reactive short chain radicals between controlled and conventional radical polymerization caused the change in branching fraction.³⁰ However both stochastic³⁵ and deterministic models²³ have shown that the chain length dependent rate constant have a minimal effect on the branching fraction. Having eliminated this, there remains several potential causes for the reduction in branching such as (i) a decrease in the backbiting reaction under controlled radical polymerization conditions (ii) a fast and virtually irreversible deactivation of the tertiary radical formed by backbiting or (iii) a combination of the above.

Reyes and Asua³⁵ used a stochastic model with arbitrary distributions for the reaction times and illustrated that the reduction in branching fraction can be caused by a decrease in the backbiting reaction because the timescale for deactivation of the active radical is faster than the timescale

for backbiting. However, these authors used Gaussian distributions for the probability density functions of the different reactions that when used in a rigorously applied stochastic process leads to the conclusion that backbiting can never occur, namely, the distributions used by Reyes and Asua cannot be used to represent competitive reactions. Conversely, Konkolewicz *et al.*²³ used a deterministic model to study the decrease of branching fraction in atom transfer radical polymerization (ATRP) of acrylates. The authors maintained a constant ratio of k_{bb}/k_p in keeping with the traditional assumption of the probability density being defined by an exponential function. It is clear that in the absence of any variation in the k_{bb}/k_p ratio the only possibility for decrease in branching fraction is that some of the tertiary radicals are deactivated irreversibly. Such a conclusion is somewhat supported by the observance of the capped tertiary radical in nitroxide mediated polymerizations of n-butyl acrylate although no decrease in branching was reported.³⁶ However, in the case of ATRP, the final polymer should contain midchain bromides, and Ballard *et al.*³³ have shown that the midchain bromides are not observable in samples of poly(n-butyl acrylate) synthesized by ATRP. Furthermore, they demonstrated that ATRP is highly efficient in chain extension from midchain bromides by using a poly(n-butyl acrylate-co-butyl 2-bromoacrylate) copolymer, a synthetic analogue of the patched midchain bromide polymer, as a macroinitiator. This proved that the irreversible capping of the midchain radical is not the cause for the branching reduction in ATRP. Therefore, the lower branching should be due to a reduction in the backbiting relative to propagation.

The reduction in branching fraction for high chain transfer agent (CTA) concentrations was attributed to a patching mechanism in which the tertiary center tends to undergo chain transfer to CTA instead of propagation.^{28,29,31} In the case of using CBr₄ as CTA, this mechanism would lead

to midchain bromides that should be observable in the final product. However, Agirre *et al.*³² showed that in the presence of large amounts of CBr_4 as chain transfer agent a significant reduction in branching fraction compared to a conventional radical polymerization was observed, but it was not possible to observe the patched structure. A closer look at this article shows the presence of a signal at 66.4 ppm that has recently been identified as belonging to the O-CH_2 carbon adjacent to a midchain bromide.³³ However, the intensity of the peak is not large enough to alter the conclusion that patching is not the reason for the reduction in branching. Therefore, similar to the case of ATRP, the lower branching should therefore be due to a smaller backbiting/propagation ratio.

The decrease in branching in high frequency PLP experiments has previously been explained by a stochastic model using similar arguments as for CRP, namely that the timescale between pulses is smaller than the timescale for backbiting.³⁷ However, in that work unrealistic Gaussian probability density functions for the reactions were used.

In this work, competitive reactions are rigorously analyzed under conditions in which the reaction time approaches the characteristic time of the slower reaction, and it is shown that a reduction in the rate of the slower process relative to faster processes is characteristic of these systems. This means that in controlled radical polymerization, radical polymerizations in the presence of high concentrations of chain transfer agents, and in high frequency PLP, reduction in branching fraction is due to reduction in the rate of backbiting with respect to propagation. The article is arranged to first give a comprehensive review of the currently applied kinetic model and its shortcomings. We then proceed to detail a new model able to account for the observed effects and finally show its application to explain experimental data, showing changes in

branching fraction in acrylic polymers synthesized by RAFT polymerization. We finally speculate on some further areas where the model may be useful to explain preexisting, apparently unexplained, data and how it may be applied for synthesis of macromolecular architectures with a higher degree of specificity than is currently possible.

Model Development

The experimental data available for the reduced branching fraction in ATRP³³ and in polymerization in the presence of high concentrations of CBr_4 ³² suggest that the reduction in the branching fraction is due to a lower backbiting rate compared with that of propagation. This result cannot be explained by classical kinetics using average rate coefficients as they predict that the instantaneous branching fraction (Equation 3) is not affected by the presence of other competitive processes. Reactions are stochastic processes and it may be argued that the average rate coefficients do not represent well such processes. However, it can be demonstrated that rigorous application of stochastics using exponential probability density functions leads to the same conclusion: the backbiting/propagation ratio should not be affected by other competing reactions (see Supporting Information).

At this point, we would like to question the validity of the exponential probability density functions to represent real processes at short times. An exponential probability density distribution predicts that the probability of reaction at time $t=0$, $p(0)$, has its highest value (see Figure 1b and 1c). This is intuitively difficult to justify since for a chemical reaction to occur, molecular rearrangement must take place which means that generally $p(0)=0$, signifying that instantaneous reaction does not occur.

To further explain this concept, let us consider a real life example. Football is a game played worldwide and with an immense volume of data available that will serve to represent the concept well. In the English Premier League, between 1994 and 2009 there were 6,706 games accounting for 603,540 minutes (assuming each game lasts 90 minutes) and during this time 17,407 goals were scored. For this large population, scoring a goal can be considered a memoryless process, namely a process in which the past does not influence the present. Statistically this is similar to a first order chemical reaction. Figure 2 shows the function of a goal being scored at a given time following the previous goal in the English Premier League between 1994 and 2009 calculated considering that the games were played consecutively. This is the probability density function of scoring goals and it is statistically equivalent to the probability density function of a reaction. It can be seen that it shows an exponential decay, typical of a first order process. However, a closer look to short times shows that, in agreement with intuition, as $t \rightarrow 0$, the probability density also goes to 0. Therefore, a better description of the data is a probability density function composed of an increasing function in the early stages followed by an exponential decay. This mathematical description can be interpreted as an event dependent on two processes that occur in series, one which dominates at very short times (in this case, the low probability of the ball reaching the goal) and the other, that dominates after this initial period (here this relates to the ‘barrier’ that prevents the goal being scored). If each of these processes were memoryless with individual probability distribution functions given by $p_i(t) = k_i e^{-k_i t}$, the probability distribution function for the completion of an individual process cycle (in this example scoring a goal) would be a hypoexponential function given by

$$p(t) = \frac{k_1 k_2}{k_2 - k_1} (e^{-k_1 t} - t e^{-k_2 t}) \quad (4)$$

This function has the shape shown by the probability distribution function for the time taken to score a goal in Figure 2. If the process cycle is the result of more than two individual sub-processes, then the hypoexponential function becomes more complex^{38–40} but retains the characteristic feature of low probability of the process occurring at short times, when compared to a single process given by a pure exponential function but with identical average rate. In this work we chose to use a hypoexponential-like function composed of a linear part and an exponential part (see Figure 3), due to its relative simplicity and its ability to represent a broad range of potential kinetic schemes, but it must be stressed that qualitatively similar results would be expected for alternative hypoexponential type functions.

The distribution described above serves to represent the fact that for any physical process the probability density distribution must tend to zero at $t=0$. In intramolecular transfer to polymer in radical polymerization of acrylates for example, a certain time is needed to form the six membered ring transition state for backbiting to occur in radical polymerization of acrylates thus a hypoexponential type probability distribution may be expected.

In the football example, the average number of goals scored per unit time is statistically equivalent to the measurable branching. The importance of the difference between the pure exponential probability density function and the hypoexponential-like one can be highlighted by a simple Monte-Carlo simulation where the time of the game is kept constant (90 minutes) but the time of each period is altered from the standard 2 halves of 45 minutes to an increased number of shorter periods (for details see Supporting Information). In Figure 2 it can be seen that

where the exponential probability density function is considered, the average number of goals per game is not affected by the length of the periods. However, in the case of the hypoexponential-like function, the average number of goals decreases as the time of the period decreases. This last prediction agrees with what any football supporter intuitively knows, that if the 90 minute games consisted of 540 periods of 10 s then the games would be essentially goalless. For periods longer than about 25 minutes there is essentially no difference between the predictions of the two distributions.

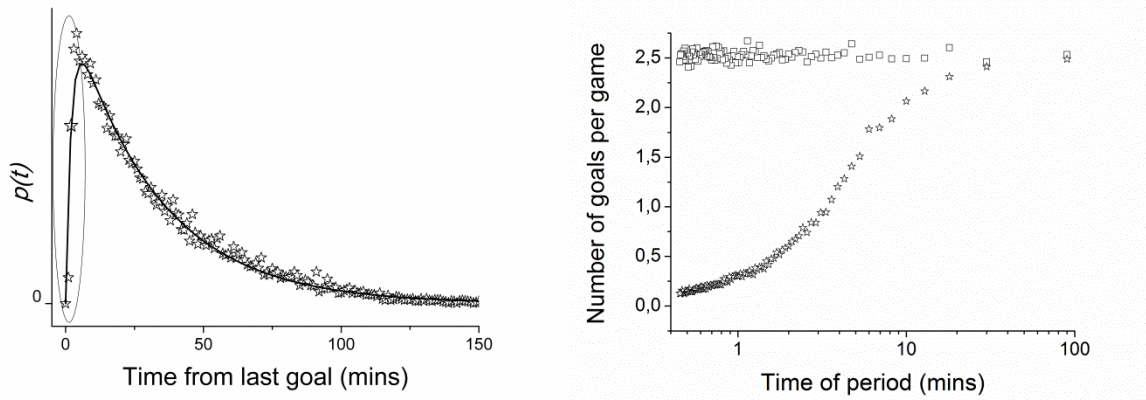


Figure 2 (Left) Probability density of a goal being scored after the previous one in the English Premier League (1994-2009). Solid line is the fit to a hypoexponential curve given by equation 4. (Right) Average number of goals per game obtained from a Monte Carlo simulation assuming a total game time of 90 minutes with different time for the periods in which they are played assuming an exponential probability density function (squares) or linear-exponential probability density function (stars).

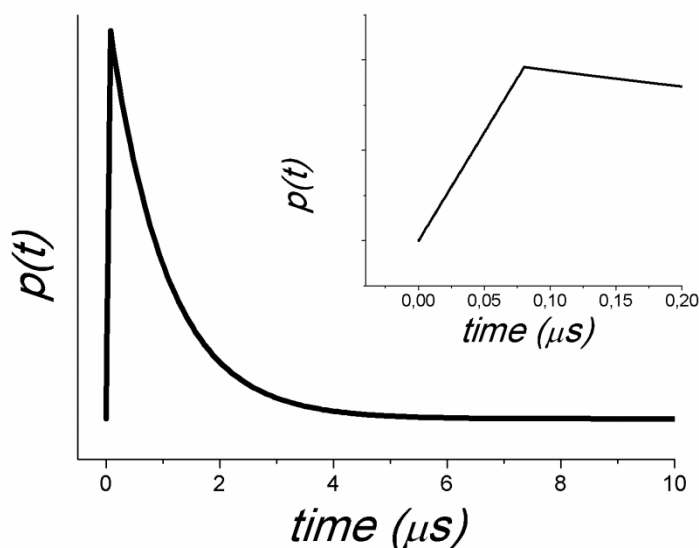


Figure 3 Example of the linear-exponential probability density function for propagation from a secondary radical. Inset shows the initial linear region of the distribution.

Analyzing polymerization processes, it is also important to bear in mind the difference in time scales between the total reaction time (typically minutes/hours for a radical polymerization) and the probability distribution function (typically 10 ms for backbiting or minutes for the football example above). With this in mind, let us now reconsider the kinetics of radical polymerization of acrylic monomers. In a conventional radical polymerization there exists a competition between several potential kinetic events a growing propagating radical can undergo, most notably propagation, termination and backbiting. The characteristic time for termination is much longer than that of propagation and backbiting and therefore it is not expected to affect the relative number of backbitings and propagations. On the other hand, in controlled radical polymerization, the introduction of an intermittent deactivation stage imposes an additional event at short times (typically $t_{deact} \ll t_{bb}$) that can radically change the relative probabilities of

backbiting and propagation if the probability distribution is not described as a simple exponential decay, as seen in the football example in Figure 2.

The probability density function depicted in Figure 3, is, for a given process i , mathematically given by

$$0 < t < t_i, p_i(t) = k_i t \quad (5)$$

$$t > t_i, p_i(t) = k_i t_i \exp\left(\frac{-t - t_i}{\tau_i}\right) \quad (6)$$

where the parameter k_i determines the gradient of the initial part of probability density function up to point in time t_i and the parameter τ_i is similar to the rate constant in classical radical kinetics, describing the decay of the exponential function in the probability density function after time t_i . The probability of a reaction having occurred by time t , $P(t)$, is therefore given by

$$P_i(t < t_i) = \int_0^t k_i t' dt' = \frac{k_i t^2}{2} \quad (7)$$

$$P_i(t > t_i) = \int_0^{t_i} k_i t' dt' + \int_{t_i}^t k_i t_i \exp\left(\frac{-t' - t_i}{\tau_i}\right) dt' = \frac{k_i t_i^2}{2} + k_i t_i \tau_i \left(1 - \exp\left(\frac{-t - t_i}{\tau_i}\right)\right) \quad (8)$$

As $t \rightarrow \infty$ then $P_i(\infty) = 1$ thus the slope of the initial part of the curve is given by

$$k_i = \frac{2}{2t_i \tau_i + t_i^2} \quad (9)$$

and the probability distribution can be rewritten as

$$0 < t < t_i, p_i(t) = \frac{2t}{2t_i \tau_i + t_i^2} \quad (10)$$

$$t > t_i, p_i(t) = \frac{2t_i}{2t_i \tau_i + t_i^2} \exp\left(\frac{-t - t_i}{\tau_i}\right) \quad (11)$$

This curve describes the probability distribution with the area beneath it being 1 and with a mean, being equal to the characteristic timescale for a reaction to occur.

$$\bar{t}_i = \int_0^{\infty} t p_i(t) dt = \frac{2}{2t_i\tau_i + t_i^2} \left(\frac{t_i^3}{3} + t_i\tau_i^2 \left(1 + \frac{t_i}{\tau_i} \right) \right) \quad (12)$$

The intrinsic rate constant for a given reaction is given by $1/\bar{t}_i$, which for propagation of secondary radicals is $k_{p,int}[M]$, for backbiting $k_{bb,int}$ and for deactivation of a propagating secondary radical by RAFT agent $k_{add,int}[RAFT]$. It is worth discussing the effect of the present theory on the relationship between the intrinsic rate coefficient and the rate coefficient determined from experimental measurements. When the kinetic rate coefficient of a given reaction is determined independently, without the influence of other processes, both the intrinsic and experimentally measured rate coefficients coincide. This is the case for the propagation rate coefficient for secondary radicals as measured by PLP ($k_p = k_{p,int}$). However, when, as in the case of backbiting, the rate coefficient is determined in the presence of other processes (i.e. propagation) then the relationship between the intrinsic and experimentally determined rate coefficient is not straightforward. This would also cause issues with the calculation of any kinetic rate constant in the presence of competitive reactions.

The experimental data used in this work (RAFT polymerization of n-butyl acrylate) showed that the reactions were not carried out under isothermal conditions. Therefore, the values of the rate coefficients k_p and k_{bb} are unknown and it was decided to normalize the coefficients by “ $k_p[M]^*$ ”, where $[M]^* = 1 \text{ mol L}^{-1}$. The normalization allows for relative probabilities to be calculated without taking into account changes in temperature throughout the polymerization and leads to a similar set of equations:

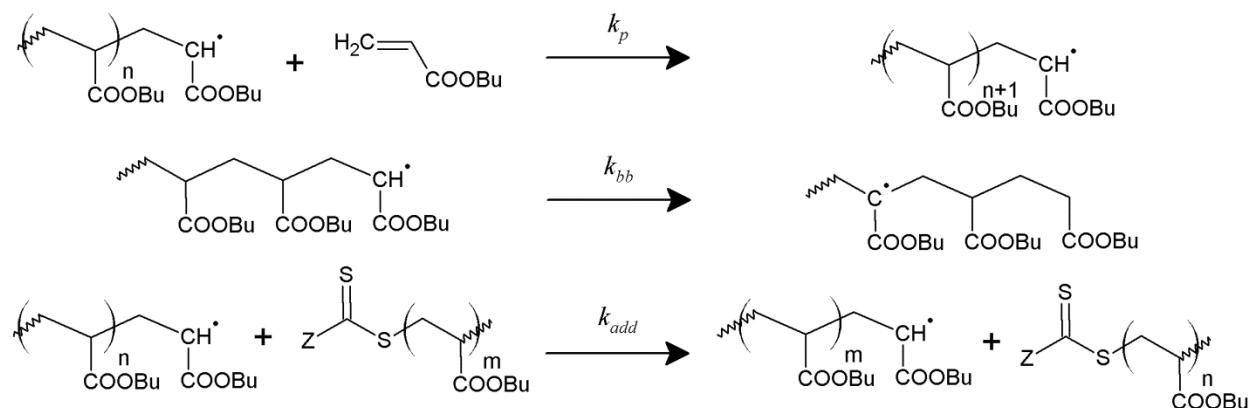
$$\text{For } 0 < t^* < t_i^* \quad p_i(t^*) = \frac{2t_i^*}{t_i^{*2} + 2t_i^* \tau_i^*}$$

(12)

$$\text{For } t^* > t_i^* \quad p_i(t^*) = \frac{2t_i^*}{t_i^{*2} + 2t_i^* \tau_i^*} \exp\left(\frac{-t^* - t_i^*}{\tau_i^*}\right) \quad (13)$$

where $t^* = t \times k_p[M]^*$; $t_i^* = t_i \times k_p[M]^*$ and $\tau_i^* = \tau_i \times k_p[M]^*$. Then the mean values of the normalized distributions are $k_p[M]^*/k_p[M] = 1/[M]$ for propagation, $k_p[M]^*/k_{bb,int}$ for backbiting and $k_p[M]^*/k_{add,int}[\text{RAFT}]$ for the addition of secondary radicals to the RAFT. Note that for propagation and deactivation, t_i^* and τ_i^* are divided by $[M]$ and $[\text{RAFT}]$ for different conversions or different experiments. The summary of the competing reactions considered in the kinetic model is shown in **Scheme 2**.

Scheme 2 Reactions scheme used for Monte-Carlo kinetic model.



EXPERIMENTAL

Materials

N-butyl acrylate (Quimidroga, technical grade) was purified by distillation and was kept at -20°C until use. The initiators, azobisisobutyronitrile (AIBN, Aldrich, 98%) and 1,1'-

azobis(cyclohexanecarbonitrile) (ACHN, Aldrich, 97%) and the RAFT agents, 2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid (DTTC, Strem, 97%), methyl 2-propionate methyl(4-pyridinyl)carbamodithioate (MPCP, Aldrich, 97%), 4-cyano-4-(phenylcarbonothioylthio)pentanoic acid (CPTP, Aldrich, 97%) were used as received. All other solvents were purchased from Scharlab and were used without purification.

Methods

NMR spectra were recorded at 25 °C in CDCl₃ at a concentration of 200mg.ml⁻¹ on a Bruker AVANCE 500 MHz equipped with a z-gradient double resonance probe. 1D ¹H spectra were acquired by use of 32k data points which were zero-filled to 64k data points prior to Fourier transformation. 1D ¹³C spectra were recorded at a ¹³C Larmor frequency of 125.77 MHz. The spectra were recorded using 20000 transients. Quantitative ¹³C spectra were recorded using single pulse excitation, using a 5.5 μs 90° pulse, inverse gated waltz16 decoupling to avoid NOE effects and a relaxation delay of 10 s. Apodization was achieved using an exponential window function equivalent to a linewidth of 10 Hz. 1D ¹³C DEPT-135 spectra were acquired for 16000 transients using single pulse excitation, using a 5.5 μs 90° pulse, inverse gated waltz16 decoupling to avoid NOE effects and a relaxation delay of 10 s. Apodization was achieved using an exponential window function equivalent to a linewidth of 3 Hz. 2D NMR spectra were recorded in HSQC and HMBC experiments. The spectral widths for the HSQC experiment were 5000 and 25000 Hz for the ¹H and the ¹³C dimensions respectively. The number of collected complex points was 2048 for the ¹H dimension with a recycle delay of 5 s. The number of transients was 64 and 256 time increments were recorded in the ¹³C dimension. The ¹J_{CH} used was 140 Hz. The J-coupling evolution delay was set to 3.2 ms. The squared cosine-bell

apodization function was applied in both dimensions. Prior to Fourier transformation the data matrices were zero filled to 1024 points in the ^{13}C dimension. The branching fraction, f_{Br} , of the polymers were calculated from quantitative ^{13}C spectra from the ratio of the integral of the quaternary carbon peak (45-49 ppm) and the methyl group of the butyl ester (11 -14 pm).⁹ The methyl group of the butyl ester was used instead of the tertiary carbon in the backbone for comparison as reported in the cited article due to the superior resolution of this peak and overlap of some peaks from the RAFT agents used with the backbone carbon signals in ^{13}C NMR. The error in the branching fraction was calculated from the inverse of the signal to noise ratio of the quaternary carbon peak. This approach is valid where the integral area of the quaternary peak is substantially smaller than the peak against which it is compared.

RAFT polymerization

RAFT polymerizations were conducted in two-neck round bottomed flasks with a fitted reflux condenser under an atmosphere of nitrogen. In a typical reaction, the RAFT agent, monomer, solvent and initiator were mixed to dissolution and then the solution was bubbled with nitrogen for 20 minutes. The bulk reactions were conducted on a 2 g scale while the solution polymerizations were conducted on a 5 g scale. The reaction was heated to reaction temperature and left for 3 hours (bulk polymerizations at 80 °C) or 1 hour (solution polymerization 110 °C). Fractional conversion, X, was calculated gravimetrically. The reactions performed are detailed in Table 1.

Table 1 Details of RAFT reactions

Temperature	Solvent	[M]	Initiator	[Initiator]	RAFT	[RAFT]	Time	X	f_{Br}^b
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(°C)	(mol L ⁻¹)			(mM)	agent ^a	(mM)	(h)		
80	Bulk	6.9	AIBN	10	-	0	3	0.80	1.82 ± 0.02
					DTTC	5.0		0.81	1.71 ± 0.14
					DTTC	100		0.69	1.34 ± 0.19
					CPTP	9.9		0.72	1.55 ± 0.08
					MPCP	12.1		0.70	2.03 ± 0.16
110	Xylene	2.25	ACHN	7.25	-	0	1	0.82	2.85 ± 0.16
					DTTC	4.5		0.80	2.39 ± 0.12
					DTTC	33		0.80	1.55 ± 0.08
					MPCP	5.4		0.82	3.09 ± 0.12
					MPCP	28		0.80	2.89± 0.16

^a RAFT agents used were 2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid (DTTC), Methyl 2-[methyl(4-pyridinyl)carbamothioylthio]propionate (MPCP), and 4-Cyano-4-(phenylcarbonothioylthio)pentanoic acid (CPTP). ^bError in branching fraction is calculated from the inverse of the signal to noise ratio of the quaternary carbon peak (see methods section).

RESULTS

The proposed model was verified experimentally by using RAFT polymerization with varying concentrations of RAFT agent to observe the difference in the branching fraction, f_{Br} , which is in turn dependent on the rate of transfer to polymer. Table 1 shows that for the trithiocarbonate RAFT agent, DTTC, in both solution and bulk polymerizations the branching fraction decreases with increasing DTTC concentration. This result is in qualitative agreement with the predictions of the linear-exponential model that states that if the deactivation time (which for a RAFT polymerization decreases as $k_{add,int}[RAFT]$ increases) decreases, then the rate of transfer to polymer relative to propagation will be reduced and therefore the branching fraction should decrease (see Figure 2b). This effect is also observable using the more active dithiobenzoate

RAFT agent, CPTP, for which the branching is reduced substantially even at low concentrations. Therefore, by changing the RAFT agent, and thus the value of rate constant $k_{add,int}$, or its concentration, the branching fraction can be reduced relative to that of radical polymerization. Similar effects have previously been observed in nitroxide mediated polymerizations by using excess of free nitroxide resulting in a lower branching fraction.³⁰ We also performed experiments with a dithiocarbamate RAFT agent (MPCP) which typically gives very poor control of acrylate polymerizations because of the low chain transfer constant. When MPCP was used, no change in the branching fraction compared to the conventional radical polymerizations was observed. In terms of the linear-exponential model this is explained by the fact that the low $k_{add,int}$ results in a long deactivation time that is of the same order of magnitude or greater than the characteristic time for backbiting and hence it will not affect the rate of backbiting.

Following these experimental observations we explored the possibility of quantitative fitting of the data to the proposed model. In order to implement this, we performed a series of Monte-Carlo simulations and the unknown parameters were estimated using a Nelder-Mead simplex algorithm for the data obtained with the trithiocarbonate RAFT agent, DTTC (see Supporting Information for the description of the algorithm). We assumed all reactions to be described by the linear-exponential density functions such that the unknown parameters were t_i^* ($i=1,2,3$ for propagation, backbiting and radical addition to RAFT agent see **Scheme 2**), $k_{bb,int}/k_p[M]^*$ and $k_{add,int}[RAFT]^*/k_p[M]^*$, where $[RAFT]^*=1 \text{ mol L}^{-1}$ and $[M]^*=1 \text{ mol L}^{-1}$. The results of the model fit to the bulk and solution polymerization data are given in Table 2.

Table 2 Results of polymerization of n-butyl acrylate and corresponding fit of model data based on parameter estimation approach.

RAFT concentration / mol L ⁻¹	Monomer Concentration / mol L ⁻¹	Experimental branching fraction / %	Model prediction branching fraction / %
0.0	6.9	1.82±0.02	1.78 ^a
5 x 10 ⁻³	6.9	1.71±0.14	1.73 ^a
100 x 10 ⁻³	6.9	1.34±0.19	1.33 ^a
0.0	2.25	2.85±0.16	2.81 ^b
4.5x 10 ⁻³	2.25	2.39±0.12	2.44 ^b
33x 10 ⁻³	2.25	1.55±0.08	1.54 ^b

^a Estimated values of the parameters $t_1^*=6.89 \times 10^{-2}$, $t_2^*=8.39 \times 10^{-2}$, $t_3^*=5.48 \times 10^{-3}$, $k_{bb,int}/k_p[M]^*=7.33 \times 10^{-2}$ and $k_{add,int}[RAFT]^*/k_p[M]^*=23.1$.

^b Estimated values of the parameters $t_1^*=7.97 \times 10^{-2}$, $t_2^*=1.28$, $t_3^*=3.85 \times 10^{-4}$, $k_{bb,int}/k_p[M]^*=6.18 \times 10^{-2}$ and $k_{add,int}[RAFT]^*/k_p[M]^*=49.6$.

The model provides a good description for the data in every case and predicts the trend of decreasing branching fraction with increasing RAFT agent concentration. Moreover, this result is universal in explaining the decrease in branching density in all controlled radical polymerizations in which the deactivation time is typically much faster than the characteristic time for backbiting. The good agreement between the model and the experimental data can be seen in Figure 4. The linear-exponential distribution model would also explain why in both pulsed laser polymerizations and in chain transfer agent mediated polymerizations branching is reduced since both introduce a competitive event that is significantly faster than the characteristic time for backbiting and will reduce its rate relative to that of propagation.

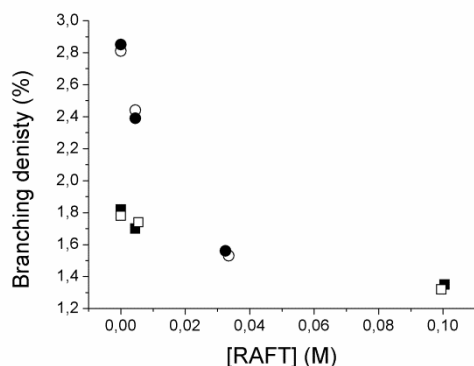


Figure 4 Agreement between model (open symbols) and experimental data (filled symbols) for branching fraction in RAFT polymerization of n-butyl acrylate at 80 °C in bulk (squares) and 110 °C in solution (circles) according to recipes in **Table 1**.

The shape of the probability density functions can evolve with conversion due to changes in the concentrations of the chemical species involved. Figure 5 shows the normalized probability density distribution for propagation, chain transfer to RAFT agent, and backbiting at low and high conversion for a RAFT solution polymerization conducted at $[M_0]=2.25 \text{ mol L}^{-1}$, $[RAFT]=33 \text{ mmol L}^{-1}$. It can be observed that at low conversion, the probability density distributions for chain transfer to RAFT agent and propagation are similar, as expected due to a similar relative rate, while the probability density distribution for backbiting has both a relatively larger linear region (indicating this process is significantly less likely to occur at short times) and has a slower exponential decay (indicating a slower average rate of reaction). At high conversion, the probability density functions for chain transfer to RAFT agent and backbiting are unchanged, since the RAFT agent concentration is constant and backbiting is concentration independent, whereas the probability density function for propagation is changed significantly and exhibits a slightly longer linear region and significantly slower decay.

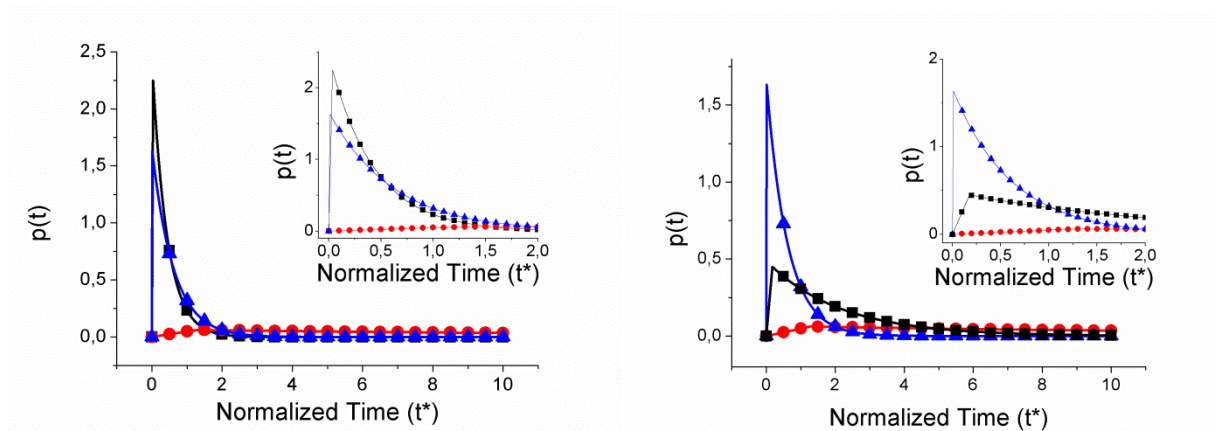


Figure 5 Changing of probability density functions from low conversion (0%, left) to high conversion (80%, right) for RAFT solution polymerization using $[M]=2.25$ M, $[RAFT]=33$ mM and parameters from results in Table 2. Propagation (squares), addition of radical to RAFT agent (triangles) and backbiting (circles). Inset shows the distributions at short times. The normalized time is given by $t^*=t \times k_p[M]^*$ where $[M]^*=1$.

Although the parameter estimation process gives a good fit to the data it must be highlighted that it is an ill-posed estimation, namely it presents more than one solution as shown in the supporting information. Therefore, at this stage it is difficult to assign these values with confidence. One of the main difficulties is that the physical origin of the timescale in which the linear part of the probability distribution function exists is not yet clear. For the effect to be of significance, the linear region timescale must be at least remotely similar to that of the average transient radical lifetime. In this case, limitations at short times due to diffusion or molecular rearrangement seem unlikely but alternative possibilities may be explored. For example, the addition of hydroxyl radicals to alkenes has been shown to proceed via a two step process involving long range transition states^{41–43} which would not be isolatable, and would not change the average rate of reaction, but would result in a hypoexponential type of probability density function as described herein.

Although the examples used in this paper focus on intramolecular chain transfer to polymer in acrylate polymerizations it is important to note that the same concept should be applicable to all kinetic events that occur in radical processes and in a broader sense to all chemical reactions. Indeed, even after a brief foray into the literature on the subject of controlled radical polymerization one will encounter numerous examples of a seemingly unexplainable reduction in reactivity or enhanced selectivity when deactivation rates are high. Table 3 summarizes these examples including the theories currently offered to explain them. This table also shows that all these findings can be explained by means of the model based on a hypoexponential probability density distribution. It is very difficult to say at this stage to what extent the current theories are incorrect (if at all), whether the proposed theory is the cause for the change in reactivity or whether the change in reactivity is due to multiple causes acting in tandem. In order to make firm statements further experimental work must come to light that is capable of discerning between these mechanisms which will be a decidedly tricky task.

In the single electron transfer-degenerative chain transfer living radical polymerization (SET-DTLRP) of vinyl chloride, for example, it has been shown that defect free samples can be prepared.⁴⁴⁻⁴⁷ In light of the theory proposed here it may be as a result of the reduced transient radical lifetime that defects, which for vinyl chloride polymerization are largely caused by transfer to polymer, are reduced. In addition, similar polymerizations conducted in aqueous media suggested that chain transfer to the poly(vinyl alcohol) stabilizer employed does not occur.^{47,48} Given that chain transfer to PVA in conventional radical polymerization of PVC is extensive and leads to a characteristic skin of the resulting particles, it is clear that the imposition of controlled polymerization conditions significantly diminishes the extent of transfer in this

case.⁴⁸ Extending further it has been shown that in general, copper(0) mediated polymerization has excellent end group fidelity in comparison to other atom transfer processes.^{49–52} Again, the current model would predict that under conditions of fast deactivation, such is the case in these polymerizations, termination and transfer events, which are typically long time scale, should be reduced with respect to propagation, thus allowing for the ultra high molecular weight polymers with near to 0 mol% termination that have been seen already. Although for acrylates this may be explained simply by the large k_p/k_t ratio, for vinyl chloride it has been shown that the molecular weight can exceed that of free radical polymerization⁴⁵ which can only be the case when molecular weight limiting reactions such as chain transfer to monomer and termination are reduced in comparison to propagation.

Extending even further, it may be considered that even short time events such as propagation may be reduced when the deactivation time is on a similar time scale to that of propagation. In the simulations conducted herein we were mainly concerned with the relative rate of propagation to backbiting that results in a reduction in branching fraction when RAFT agents were used but the rates of polymerization were also calculated. Retardation phenomena have been reported in RAFT polymerizations when certain RAFT agents are used, particularly the highly active dithiobenzoates, and the cause of this is the subject of an unresolved debate in the literature.^{53,54}

Figure 6 shows the results from the Monte Carlo simulations that predict the change in the polymerization rate for varying concentration of RAFT agent relative to the rate of polymerization for a conventional radical polymerization using the parameters estimated for the solution polymerization experiments. The results have been calculated for solution

polymerization, assuming instantaneous fragmentation of the RAFT intermediate and represent the average propagation rate between 0 and 0.82 conversion according to

$$\text{relative average propagation rate} = \frac{k_p[M]}{(k_p[M])_{\text{RAFT}=0}}$$

The rate of polymerization was calculated taking into account the complete kinetic scheme including backbiting and propagation from the tertiary radical but does not include effects due to slow fragmentation of the RAFT agent or termination of RAFT adduct radicals. It can clearly be observed that, in keeping with experimental observations, the theory qualitatively predicts that the relative rate of propagation is reduced compared to the free radical case.

Such a prediction would mean a reevaluation of the fundamental principle on which the kinetics of controlled radical polymerization are built, in that it would appear that while rate coefficients calculated from conventional radical polymerizations may be applicable in some instances, the short lifetime of the transient radical may cause significant differences in relative rates. The application of this single concept conveniently explains a number of ongoing debates and unexplained phenomena in the field of radical polymerization as summarized in **Table 3**. In light of the proposed model, it would appear that polymerization under conditions of high deactivation rates may allow for polymerizations of increased specificity with decreased termination and decreased chain transfer events thus allowing for synthesis of polymers with precise, predetermined microstructure.

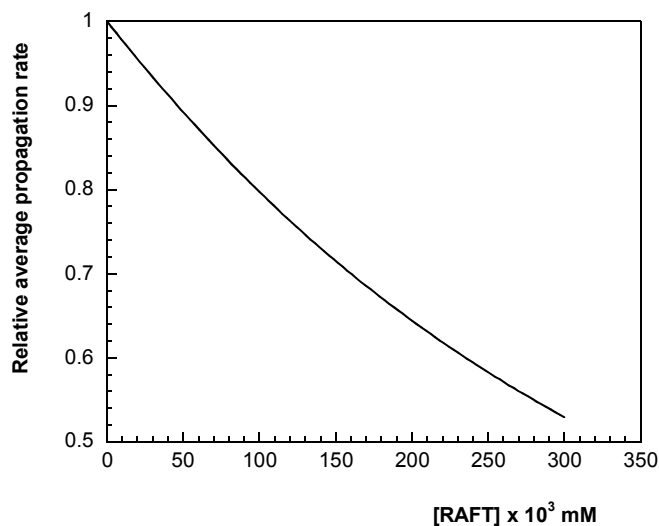


Figure 6 Predicted change in relative rate of polymerization compared to conventional radical polymerization with increasing RAFT agent concentration for solution polymerization ([M]=2.25M and using parameters given in **Table 2**).

Table 3 Unresolved/ongoing debates within controlled radical polymerization that can be conveniently explained with the linear-exponential distribution model

Observation	Current explanation(s)	Linear-Exponential probability distribution explanation
Branching reduced in controlled radical polymerization ³⁰	Irreversible deactivation of midchain radical (applied to ATRP only) ²³ (note : experimental evidence shows no irreversible deactivation of midchain radical) ³³	Intermittent deactivation of transient radical results in decrease in rate of backbiting relative to propagation
Branching reduced when high concentrations of chain transfer agent used in radical polymerization ^{31,32}	Midchain radical 'patched' by chain transfer to CTA ³¹ (note : experimental evidence does not show patched midchain radical) ³²	Reduction in radical lifetime due to chain transfer to CTA results in decrease in backbiting rate
Pulsed laser polymerization of acrylates	Fast pulse prevents formation of	Reduction in radical lifetime due to

at high frequency gives accurate k_p values at high temperatures ³⁴	excessive amounts of midchain radicals ³⁴	chain termination induced by fast laser pulse results in decrease in backbiting rate
Reduction in rate of polymerization in RAFT mediated polymerizations ^{53,54}	Either (i) Termination/Side reactions of intermediate RAFT adduct ⁵⁵⁻⁵⁷ or (ii) Slow fragmentation of intermediate RAFT adduct ⁵⁸	High deactivation rate for certain RAFT agents reduces the transient radical lifetime so $\tau_{deactivation} \approx \tau_{propagation}$ reducing propagation rate
Defect free poly(vinyl chloride) formed by SET-DTLRP ⁴⁵	Low reactions temperatures/irreversible deactivation of midchain radicals that can lead to chain transfer and branching ⁴⁷	Reduction in transient radical lifetime due to degenerative transfer process results in decrease in chain transfer to polymer and other side reactions
Absence of chain transfer to PVA in SET-DTLRP of PVC in aqueous media ⁴⁸	Not available	
High chain end fidelity/near zero termination in copper(0) mediated radical polymerizations ^{49,52,59} Ultrahigh M_w polymers possible with copper(0) mediated radical polymerizations/SET-DTLRP ^{45,50}	Low termination rates due to (i) low copper concentrations ⁶⁰ and (ii) low termination rate coefficients relative to propagation of monomers employed ^{61,62}	High deactivation rate suppresses termination and chain transfer processes

CONCLUSION

In conclusion, we have presented a new model for the relative reactivity in the presence of competitive processes that shows that under conditions of rapid radical deactivation long scale processes such as transfer to polymer can be suppressed. This model is particularly useful for explaining the enhanced selectivity of radicals in the presence of a reversible deactivation process in radical polymerization. We have shown that, based on the use of a hypoexponential-

like probability density function, good agreement between the model and experimental data for branching in RAFT polymerization of acrylic monomers is given. In addition, we have highlighted the possibility for the application of the model to various other kinetic processes in radical polymerizations. Thus using a single concept a broad range of unresolved debates can be explained. It is important to note that the model presented should be generally applicable to all chemical reactions. Application of the knowledge provided by such a model should allow for the development of highly selective radical polymerization processes potentially avoiding all chain transfer and termination events.

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REFERENCES

- (1) Plessis, C.; Arzamendi, G.; Leiza, J. R.; Schoonbrood, H. A. S.; Charmot, D.; Asua, J. M. Seeded Semibatch Emulsion Polymerization of n -Butyl Acrylate. Kinetics and Structural Properties *Macromolecules* **2000**, *33*, 5041–5047.
- (2) Plessis, C.; Arzamendi, G.; Leiza, J. R.; Schoonbrood, H. A. S.; Charmot, D.; Asua, J. M. A Decrease in Effective Acrylate Propagation Rate Constants Caused by Intramolecular Chain Transfer *Macromolecules* **2000**, *33*, 4–7.
- (3) Plessis, C.; Arzamendi, G.; Leiza, J. R.; Schoonbrood, H. A. S.; Charmot, D.; Asua, J. . Kinetics and Polymer Microstructure of the Seeded Semibatch Emulsion

- Copolymerization of n -Butyl Acrylate and Styrene *Macromolecules* **2001**, *34*, 5147–5157.
- (4) Plessis, C.; Arzamendi, G.; Alberdi, J. M.; van Herk, A. M.; Leiza, J. R.; Asua, J. M. Evidence of Branching in Poly(butyl acrylate) Produced in Pulsed-Laser Polymerization Experiments *Macromol. Rapid Commun.* **2003**, *24*, 173–177.
 - (5) Sato, E.; Emoto, T.; Zetterlund, P. B.; Yamada, B. Influence of Mid-Chain Radicals on Acrylate Free Radical Polymerization: Effect of Ester Alkyl Group *Macromol. Chem. Phys.* **2004**, *205*, 1829–1839.
 - (6) Nikitin, A. N.; Hutchinson, R. A. The Effect of Intramolecular Transfer to Polymer on Stationary Free Radical Polymerization of Alkyl Acrylates *Macromolecules* **2005**, *38*, 1581–1590.
 - (7) González, I.; Leiza, R.; Asua, M. Exploring the Limits of Branching and Gel Content in the Emulsion Polymerization of n -BA *Macromolecules* **2006**, *39*, 5015–5020.
 - (8) González, I.; Asua, J. M.; Leiza, J. R. The role of methyl methacrylate on branching and gel formation in the emulsion copolymerization of BA/MMA *Polymer* **2007**, *48*, 2542–2547.
 - (9) Castignolles, P.; Graf, R.; Parkinson, M.; Wilhelm, M.; Gaborieau, M. Detection and quantification of branching in polyacrylates by size-exclusion chromatography (SEC) and melt-state ¹³C NMR spectroscopy *Polymer* **2009**, *50*, 2373–2383.
 - (10) Liang, K.; Hutchinson, R. A.; Barth, J.; Samrock, S.; Buback, M. Reduced Branching in Poly (butyl acrylate) via Solution Radical Polymerization in n -Butanol *Macromolecules* **2011**, *44*, 5843–5845.
 - (11) Yu-Su, S. Y.; Sun, F. C.; Sheiko, S. S.; Konkolewicz, D.; Lee, H.; Matyjaszewski, K. Molecular Imaging and Analysis of Branching Topology in Polyacrylates by Atomic Force Microscopy *Macromolecules* **2011**, *44*, 5928–5936.
 - (12) Agirre, A.; Santos, J. I.; Leiza, J. R. Toward Understanding the Architecture (Branching and MWD) of Crosslinked Acrylic Latexes *Macromol. Chem. Phys.* **2013**, *214*, 589–598.
 - (13) Ahmad, N. M.; Heatley, F.; Lovell, P. A. Chain Transfer to Polymer in Free-Radical Solution Polymerization of n -Butyl Acrylate Studied by NMR Spectroscopy *Macromolecules* **1998**, *31*, 2822–2827.
 - (14) Farcet, C.; Belleney, J.; Charleux, B.; Pirri, R. Structural Characterization of Nitroxide-Terminated Poly (n -butyl acrylate) Prepared in Bulk and Miniemulsion Polymerizations *Macromolecules* **2002**, *35*, 4912–4918.

- (15) Junkers, T.; Barner-Kowollik, C. The Role of Mid-Chain Radicals in Acrylate Free Radical *J. Polym. Sci. Part A Polym. Chem.* **2008**, *46*, 7585–7605.
- (16) Buback, M.; Hesse, P.; Junkers, T.; Sergeeva, T.; Theis, T. PLP Labeling in ESR Spectroscopic Analysis of Secondary and Tertiary Acrylate Propagating Radicals *Macromolecules* **2008**, *41*, 288–291.
- (17) Cuccato, D.; Mavroudakos, E.; Dossi, M.; Moscatelli, D. A Density Functional Theory Study of Secondary Reactions in n -Butyl Acrylate Free Radical Polymerization *Macromol. Theory Simulations* **2013**, *22*, 127–135.
- (18) Heatley, F.; Lovell, P. A.; Yamashita, T. Chain Transfer to Polymer in Free-Radical Solution Polymerization of 2-Ethylhexyl Acrylate Studied by NMR Spectroscopy *Macromolecules* **2001**, *34*, 7636–7641.
- (19) Thickett, S. C.; Gilbert, R. G. Midchain Transfer to Polymer in Styrene-Poly(butyl acrylate) Systems : Direct Evidence of Retardative Effects *Macromolecules* **2005**, *38*, 9894–9896.
- (20) Van Herk, A. M. Historic account of the development in the understanding of the propagation kinetics of acrylate radical polymerizations. *Macromol. Rapid Commun.* **2009**, *30*, 1964–1968.
- (21) Van Herk, A. M. Pulsed Initiation Polymerization Applied to Acrylate Monomers: Sources of Experimental Failure *Macromol. Rapid Commun.* **2001**, *22*, 687–689.
- (22) Willemse, R. X. E.; Herk, A. M. Van; Panchenko, E.; Junkers, T.; Buback, M. PLP - ESR Monitoring of Midchain Radicals in n -Butyl Acrylate Polymerization *Macromolecules* **2005**, *38*, 5098–5103.
- (23) Konkolewicz, D.; Sosnowski, S.; D'hooge, D. R.; Szymanski, R.; Reyniers, M.-F.; Marin, G. B.; Matyjaszewski, K. Origin of the Difference between Branching in Acrylates Polymerization under Controlled and Free Radical Conditions: A Computational Study of Competitive Processes *Macromolecules* **2011**, *44*, 8361–8373.
- (24) Peck, A. N. F.; Hutchinson, R. A. Secondary Reactions in the High-Temperature Free Radical Polymerization of Butyl Acrylate *Macromolecules* **2004**, *37*, 5944–5951.
- (25) Nikitin, A. N.; Hutchinson, R. A.; Buback, M.; Hesse, P. Determination of Intramolecular Chain Transfer and Midchain Radical Propagation Rate Coefficients for Butyl Acrylate by Pulsed Laser Polymerization *Macromolecules* **2007**, *40*, 8631–8641.

- (26) Arzamendi, G.; Plessis, C.; Leiza, J. R.; Asua, J. M. Effect of the Intramolecular Chain Transfer to Polymer on PLP/SEC Experiments of Alkyl Acrylates *Macromol. Theory Simulations* **2003**, *12*, 315–324.
- (27) Plessis, C.; Arzamendi, G.; Leiza, R.; Schoonbrood, H. A. S.; Charmot, D.; Asua, M. Modeling of Seeded Semibatch Emulsion Polymerization of n -BA *Ind. Eng. Chem. Res.* **2001**, *40*, 3883–3894.
- (28) Junkers, T.; Koo, S. P. S.; Davis, T. P.; Stenzel, M. H.; Barner-Kowollik, C. Mapping Poly(butyl acrylate) Product Distributions by Mass Spectrometry in a Wide Temperature Range: Suppression of Midchain Radical Side Reactions *Macromolecules* **2007**, *40*, 8906–8912.
- (29) Koo, S. P. S.; Junkers, T.; Barner-Kowollik, C. Quantitative Product Spectrum Analysis of Poly(butyl acrylate) via Electrospray Ionization Mass Spectrometry *Macromolecules* **2009**, *42*, 62–69.
- (30) Ahmad, N. M.; Charleux, B.; Farcet, C.; Ferguson, C. J.; Gaynor, S. G.; Hawket, B. S.; Heatley, F.; Klumperman, B.; Konkolewicz, D.; Lovell, P. A.; Matyjaszewski, K.; Venkatesh, R. Chain Transfer to Polymer and Branching in Controlled Radical Polymerizations of n-Butyl Acrylate. *Macromol. Rapid Commun.* **2009**, *30*, 2002–2021.
- (31) Gaborieau, M.; Koo, S. P. S.; Castignolles, P.; Junkers, T.; Barner-Kowollik, C. Reducing the Degree of Branching in Polyacrylates via Midchain Radical Patching: A Quantitative Melt-State NMR Study *Macromolecules* **2010**, *43*, 5492–5495.
- (32) Agirre, A.; Santos, J. I.; Etxeberria, A.; Sauerland, V.; Leiza, J. R. Polymerization of n-butyl acrylate with high concentration of a chain transfer agent (CBr₄): detailed characterization and impact on branching *Polym. Chem.* **2013**, *4*, 2062–2079.
- (33) Ballard, N.; Salsamendi, M.; Santos, J. I.; Ruipérez, F.; Leiza, J. R.; Asua, J. M. Experimental Evidence Shedding Light on the Origin of the Reduction of Branching of Acrylates in ATRP *Macromolecules* **2014**, *47*, 964–972.
- (34) Barner-Kowollik, C.; Günzler, F.; Junkers, T. Pushing the Limit - Pulsed Laser Polymerization of n -Butyl Acrylate at 500 Hz *Macromolecules* **2008**, *41*, 8971–8973.
- (35) Reyes, Y.; Asua, J. M. Revisiting chain transfer to polymer and branching in controlled radical polymerization of butyl acrylate. *Macromol. Rapid Commun.* **2011**, *32*, 63–67.
- (36) Hlalele, L.; Klumperman, B. Reversible Nitroxide Trapping of the Mid-Chain Radical in n -Butyl Acrylate Polymerization *Macromolecules* **2011**, *44*, 5554–5557.

- (37) Reyes, Y.; Arzamendi, G.; Asua, J. M.; Leiza, J. R. Branching at High Frequency Pulsed Laser Polymerizations of Acrylate Monomers *Macromolecules* **2011**, *44*, 3674–3679.
- (38) Kou, S. C.; Cherayil, B. J.; Min, W.; English, B. P.; Xie, X. S. Single-molecule Michaelis-Menten equations. *J. Phys. Chem. B* **2005**, *109*, 19068–19081.
- (39) Zhou, Y.; Zhuang, X. Kinetic analysis of sequential multistep reactions. *J. Phys. Chem. B* **2007**, *111*, 13600–13610.
- (40) Floyd, D. L.; Harrison, S. C.; van Oijen, A. M. Analysis of kinetic intermediates in single-particle dwell-time distributions. *Biophys. J.* **2010**, *99*, 360–366.
- (41) Daranlot, J.; Bergeat, A.; Caralp, F.; Caubet, P.; Costes, M.; Forst, W.; Loison, J.-C.; Hickson, K. M. Gas-phase kinetics of hydroxyl radical reactions with alkenes: experiment and theory. *Chemphyschem* **2010**, *11*, 4002–4010.
- (42) Greenwald, E. E.; North, S. W.; Georgievskii, Y.; Klippenstein, S. J. A two transition state model for radical-molecule reactions: a case study of the addition of OH to C₂H₄. *J. Phys. Chem. A* **2005**, *109*, 6031–6044.
- (43) Greenwald, E. E.; North, S. W.; Georgievskii, Y.; Klippenstein, S. J. A two transition state model for radical-molecule reactions: applications to isomeric branching in the OH-isoprene reaction. *J. Phys. Chem. A* **2007**, *111*, 5582–5592.
- (44) Coelho, J. F. J.; Fonseca, a. C.; Gois, J. R.; Gonçalves, P. M. O. F.; Popov, A. V.; Gil, M. H. Scaling-up of poly(vinyl chloride) prepared by single electron transfer degenerative chain transfer mediated living radical polymerization in water media: 1) Low molecular weight. Kinetic analysis *Chem. Eng. J.* **2011**, *169*, 399–413.
- (45) Percec, V.; Ramirez-Castillo, E.; Hinojosa-Falcon, L. A.; Popov, A. V. Synthesis of ultrahigh molar mass, structural defects free poly(vinyl chloride) with high syndiotacticity and glass transition temperature by single electron transfer-degenerative chain transfer living radical polymerization (SET-DTLRP) *J. Polym. Sci. Part A Polym. Chem.* **2005**, *43*, 2185–2187.
- (46) Percec, V.; Popov, A. V.; Ramirez-Castillo, E.; Weichold, O. Acceleration of the single electron transfer-degenerative chain transfer mediated living radical polymerization (SET-DTLRP) of vinyl chloride in water at 25 °C *J. Polym. Sci. Part A Polym. Chem.* **2004**, *42*, 6364–6374.
- (47) Percec, V.; Popov, A. V.; Ramirez-Castillo, E.; Coelho, J. F. J.; Hinojosa-Falcon, L. a. Non-transition metal-catalyzed living radical polymerization of vinyl chloride initiated with iodoform in water at 25 °C *J. Polym. Sci. Part A Polym. Chem.* **2004**, *42*, 6267–6282.

- (48) Coelho, J. F. J.; Fonseca, A. C.; Gonçalves, P. M. F. O.; Popov, A. V.; Gil, M. H. Particle features and morphology of poly(vinyl chloride) prepared by living radical polymerisation in aqueous media. Insight about particle formation mechanism *Polymer* **2011**, *52*, 2998–3010.
- (49) Nyström, F.; Soeriyadi, A. H.; Boyer, C.; Zetterlund, P. B.; Whittaker, M. R. End-group fidelity of copper(0)-mediated radical polymerization at high monomer conversion: an ESI-MS investigation *J. Polym. Sci. Part A Polym. Chem.* **2011**, *49*, 5313–5321.
- (50) Percec, V.; Guliashvili, T.; Ladislaw, J. S.; Wistrand, A.; Stjern Dahl, A.; Sienkowska, M. J.; Monteiro, M. J.; Sahoo, S. Ultrafast synthesis of ultrahigh molar mass polymers by metal-catalyzed living radical polymerization of acrylates, methacrylates, and vinyl chloride mediated by SET at 25 degrees C. *J. Am. Chem. Soc.* **2006**, *128*, 14156–14165.
- (51) Nguyen, N. H.; Levere, M. E.; Percec, V. SET-LRP of methyl acrylate to complete conversion with zero termination *J. Polym. Sci. Part A Polym. Chem.* **2012**, *50*, 860–873.
- (52) Jakubowski, W.; Kirci-Denizli, B.; Gil, R. R.; Matyjaszewski, K. Polystyrene with Improved Chain-End Functionality and Higher Molecular Weight by ARGET ATRP *Macromol. Chem. Phys.* **2008**, *209*, 32–39.
- (53) Barner-kowollik, C.; Buback, M.; Charleux, B.; Coote, M. L.; Drache, M.; Fukuda, T.; Goto, A.; Klumperman, B.; Lowe, A. B.; Mcleary, J. B.; Moad, G.; Monteiro, M. J.; Sanderson, R. D.; Tonge, M. P.; Vana, P.; Marie, P. Mechanism and Kinetics of Dithiobenzoate-Mediated RAFT Polymerization . I . The Current Situation *J. Polym. Sci. Part A Polym. Chem.* **2006**, *44*, 5809–5831.
- (54) Moad, G. Mechanism and Kinetics of Dithiobenzoate-Mediated RAFT Polymerization - Status of the Dilemma *Macromol. Chem. Phys.* **2014**, *215*, 9–26.
- (55) Geelen, P.; Klumperman, B. Intermediate Radical Termination in Reversible Addition-Fragmentation Chain Transfer-Mediated Polymerization : Identification of Termination Products *Macromolecules* **2007**, *40*, 3914–3920.
- (56) Calitz, F. M.; McLeary, J. B.; McKenzie, J. M.; Tonge, M. P.; Klumperman, B.; Sanderson, R. D. Evidence for Termination of Intermediate Radical Species in RAFT-Mediated Polymerization *Macromolecules* **2003**, *36*, 9687–9690.
- (57) Konkolewicz, D.; Hawket, B. S.; Gray-Weale, A.; Perrier, S. RAFT Polymerization Kinetics: Combination of Apparently Conflicting Models *Macromolecules* **2008**, *41*, 6400–6412.

- (58) Feldermann, A.; Coote, M. L.; Stenzel, M. H.; Davis, T. P.; Barner-Kowollik, C. Consistent experimental and theoretical evidence for long-lived intermediate radicals in living free radical polymerization. *J. Am. Chem. Soc.* **2004**, *126*, 15915–15923.
- (59) Soeriyadi, A. H.; Boyer, C.; Nyström, F.; Zetterlund, P. B.; Whittaker, M. R. High-order multiblock copolymers via iterative Cu(0)-mediated radical polymerizations (SET-LRP): toward biological precision. *J. Am. Chem. Soc.* **2011**, *133*, 11128–11131.
- (60) Wang, Y.; Soerensen, N.; Zhong, M.; Schroeder, H.; Buback, M.; Matyjaszewski, K. Improving the “Livingness” of ATRP by Reducing Cu Catalyst Concentration *Macromolecules* **2013**, *46*, 683–691.
- (61) Zhong, M.; Matyjaszewski, K. How Fast Can a CRP Be Conducted with Preserved Chain End Functionality? *Macromolecules* **2011**, *44*, 2668–2677.
- (62) Konkolewicz, D.; Wang, Y.; Zhong, M.; Krys, P.; Isse, A. A.; Gennaro, A.; Matyjaszewski, K. Reversible-Deactivation Radical Polymerization in the Presence of Metallic Copper. A Critical Assessment of the SARA ATRP and SET-LRP Mechanisms *Macromolecules* **2013**, *46*, 8749–8772.

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